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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,269	07/08/2008	Shaomeng Wang	UM-13022	8028

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,269	WANG ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20080326; 20070821; 20070521*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due

under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

Amino acid sequences subject to the sequence disclosure rules are present in, e.g., paragraphs [0010], [0011], [0121], [0125], [0130] - [0132], [0135], [0136], [0138], and [0146] of the specification. However, no sequence listing has been submitted.

Applicant must provide an original computer readable form (CRF) copy of the Sequence Listing, an original paper copy of the Sequence Listing as well as an amendment directing its

entry into the specification, and a statement that the content of the paper and computer readable copies are the same and include no new matter as required by 37 CFR 1.821(f) and (g).

3. Claims 3, 6, 9, 15, and 25 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The fourth-listed compound in claim 3 comprises a cycloalkyl-alkyl group at the position corresponding to R_2 of Formula I. However, as defined in claim 1, R_2 is not permitted to be a cycloalkyl-alkyl group. Claim 3 at page 70, last two lines, recites compounds comprising a cycloalkyl-alkyl group at the position corresponding to R_3 of Formula I. However, as defined in claim 1, R_3 is not permitted to be a cycloalkyl-alkyl group. Accordingly, claim 3 embraces compounds not embraced by the independent claim, and therefore is an improper dependent claim. For analogous reasons, dependent claims 6, 9, 15, and 25 embrace compounds not embraced by the independent claim, and therefore are improper dependent claims.

4. Claims 21-23 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative only. See MPEP § 608.01(n), and especially the example at (I)(B)(3). Note that each of claims 21-23 refers to claim 16 and to claim 1.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

6. Claims 1, 2, 4, 5, 7, 8, 10-14, and 16-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (U.S. Patent No. 6,608,026). Wang et al teach Hid-4/SEQ ID NO:15, which corresponds to Applicants' Formula I in which R_1 is C_1 alkyl, R_2 is branched alkyl, Y is CH_2, Z is CONH, and R_3 is substituted alkylaryl. The compounds of Wang et al are apoptosis enhancers, and are administered in combination with chemotherapeutic agents or radiation in

order to treat cancer. See, e.g., the Abstract; column 11, line 43 - column 12, line 9; Table 4; and claims 2-6.

7. Claims 26-30 are rejected under 35 U.S.C. 103(a) as being obvious over Wang et al (U.S. Patent No. 6,608,026). Application of Wang et al is the same as in the above rejection of claims 1, 2, 4, 5, 7, 8, 10-14, and 16-24. Wang et al do not teach their apoptosis enhancers in kit form in combination with chemotherapeutic agents and instructions for use. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to package the apoptosis enhancers of Wang et al in kit form with the chemotherapeutic agents of Wang et al and with instructions for use, because kits comprising therapeutic agents and instructions for use are commonly used in the therapeutic arts for ease of storage, transportation, measurement, and administration.

8. Claims 1, 2, 4, 5, 7, 8, 10-12, 14, 16, 17, 19, 20, 24, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 2004/005248. The WO Patent Application '248 teaches XIAP inhibitors used to treat proliferative disorders, including cancer. The inhibitors can be co-administered with other anti-cancer agents The XIAP inhibitors can be packaged in containers, ampoules, and vials. Examples 2-6 of the WO Patent Application '248 meet the requirements of Applicants' Formula I, and in particular Example 2 of the WO Patent Application '248 is the same compound as is recited in Applicants' claim 3, page 70, line 1. See also, e.g., the Abstract; page 10, lines 12-13; and page 11, line 25 - page 12, line 14. The containers, ampoules, and vials of the WO Patent Application '248 correspond to Applicants' kits.

9. Claims 3, 6, 9, 15, and 25 are rejected under 35 U.S.C. 103(a) as being obvious over the

WO Patent Application 2004/005248 as applied against claims 1, 2, 4, 5, 7, 8, 10-12, 14, 16, 17, 19, 20, 24, and 26 above, and further in view of Dyrsting et al (U.S. Patent No. 6,077,822). The WO Patent Application '248 does not teach its Example 2 compound in the form of a hydrochloride salt, although the WO Patent Application '248 does teach the general use of salt forms, including hydrochloride salt forms, of its compounds. See page 7, lines 15-25. Dyrsting et al teach that it is common practice in the pharmaceutical industry to use salt forms of drugs, including hydrogen chloride salts, for benefits such as higher solubility and greater biotolerability. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use a hydrochloride form of the Example 2 compound of the WO Patent Application '248, because the WO Patent Application '248 discloses the general utility of the salt forms of its compounds, and because Dyrsting et al teach that salt forms of drugs are common in the pharmaceutical arts and can have the benefits of higher solubility and greater biotolerability.

10. Claims 13, 18, and 21-23 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 2004/005248 as applied against claims 1, 2, 4, 5, 7, 8, 10-12, 14, 16, 17, 19, 20, 24, and 26 above, and further in view of Wang et al (U.S. Patent No. 6,608,026). The WO Patent Application '248 teaches the use of its XIAP inhibitors, optionally in conjunction with other anti-cancer agents, in order to treat cancer, but does not teach the use of its XIAP inhibitors in conjunction with radiation, and does not teach the sequence of administration for its disclosed combination of XIAP inhibitors and anti-cancer agents. Wang et al teach a method of using compounds which are IAP inhibitors and which promote apoptosis in order to treat cancer. Wang et al's compounds are administered in combination with chemotherapeutic agents or

radiation in order to treat cancer. See, e.g., the Abstract; column 11, line 43 - column 12, line 9; and claims 2-6. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the XIAP inhibitors of the WO Patent Application '248 in conjunction with radiation, because it is desirable to increase apoptosis in cancer cells regardless of the anti-cancer agent being administered to the cancer cells, because the similarity in structure and function between the XIAP inhibitors of the WO Patent Application '248 and the IAP inhibitors of Wang et al would indicate to one of ordinary skill in the art that pharmaceutical techniques useful for administration of the latter would also be useful for administration of the former, and because Wang et al teach that it is known to administer IAP inhibitors in conjunction with radiation for the treatment of cancer. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the XIAP inhibitors of the WO Patent Application '248 prior to, concurrently with, or after the administration of the other anti-cancer agents, because Wang et al teach that these are known administration schedules for the administration of IAP inhibitors and anti-cancer agents, and because it is routine in the pharmaceutical arts to determine operable and optimal administration schedules.

11. Claims 27-30 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 2004/005248. Application of the WO Patent Application '248 is the same as in the above rejection of claims 1, 2, 4, 5, 7, 8, 10-12, 14, 16, 17, 19, 20, 24, and 26. The WO Patent Application '248 does not teach the apoptosis enhancers in kit form in combination with chemotherapeutic agents and instructions for use. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to package the apoptosis enhancers of the WO Patent Application '248 in kit form with the anti-cancer agents of the WO Patent

Application '248 and with instructions for use, because kits comprising therapeutic agents and instructions for use are commonly used in the therapeutic arts for ease of storage, transportation, measurement, and administration.

12. Claims 3, 6, 9, 15, and 25 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 2004/005248. Application of the WO Patent Application '248 is the same as in the above rejection of claims 1, 2, 4, 5, 7, 8, 10-12, 14, 16, 17, 19, 20, 24, and 26. The WO Patent Application '248 in Example 5 teaches an XIAP inhibitor which differs from the compounds in Applicants' claim 3, page 70, second through fifth lines, only with respect to the identity of the alkyl or cycloalkyl-alkyl group which is attached to the C-terminal amide group. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form compounds according to Example 5 of the WO Patent Application '248 in which the branched C_5 alkyl is replaced with a branched C_4 or C_6 alkyl or with a C_3- or C_6-cycloalkyl-methyl group, because such substituents are generically encompassed by the WO Patent Application '248 definition of R_5, because such substituents differ only by the number of carbon atoms within the genus of alkyl groups, and because the resultant compounds appear to have only the activity that would have been expected in view of the WO Patent Application '248.

13. Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being obvious over the Sun et al article (J. Med. Chem., Vol. 47, pages 4147-4150). The Sun et al article teaches compound 1 (see Scheme 1) which are XIAP inhibitors (see Table 1). Compound 1 has the same structure as the compound recited at Applicants' claim 3, page 70, line 1, with the exception that Applicants' compound is in salt form. However, instant claims 1 and 2 do not require the compounds to be in salt form.

14. Claim 3 is rejected under 35 U.S.C. 103(a) as being obvious over the Sun et al article (J. Med. Chem., Vol. 47, pages 4147-4150) as applied against claims 1 and 2 above, and further in view of Dyrsting et al (U.S. Patent No. 6,077,822). The Sun et al article does not teach compound 1 in the form of a hydrochloride salt. Dyrsting et al teach that it is common practice in the pharmaceutical industry to use salt forms of drugs, including hydrogen chloride salts, for benefits such as higher solubility and greater biotolerability. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use a hydrochloride form of compound 1 of the Sun et al article, because Dyrsting et al teach that salt forms of drugs are common in the pharmaceutical arts and can have the benefits of higher solubility and greater biotolerability.

15. Applicants are requested to check in the filing receipt the spelling of the given names of Inventors Sun and Chen. Although the spellings seem to be the same as those given in the declaration filed July 8, 2008, they may not be correct.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
February 24, 2010